

CLAIMS

WE CLAIM:

Sub B²

1. A method for identifying a modulator of a protein that comprises a metalloprotease domain and a
5 thrombospondin domain, the method comprising the steps of: treating a target organism having a developing gonadal cell responsive to the protein with at least one potential modulator of cell migration; and observing in the treated target organism a change in
10 migration or shape of the developing gonadal cell attributable to the presence of the at least one modulator.

2. A method as claimed in Claim 1 wherein migration of the developing gonadal cell in the target organism before treatment is absent or reduced relative to a wild
15 type individual.

3. A method as claimed in Claim 1 wherein the treating step restores or enhances migration in the target organism relative to migration before the treating step.

4. A method as claimed in Claim 1 wherein migration
20 of the developing gonadal cell in the target organism before treatment is at a level of a wild type individual.

5. A method as claimed in Claim 1 wherein the treating step reduces migration in the target organism relative to migration before the treating step.

6. A method as claimed in Claim 1 wherein the target organism comprises a protein that comprises a metalloprotease domain and a thrombospondin domain, the protein being selected from the group consisting of a
5 protein encoded by a native polynucleotide coding sequence, a protein encoded by a heterologous polynucleotide coding sequence introduced into the target organism, a protein that shares at least 20% amino acid sequence identity with either of the foregoing and retains an ability to direct
10 cell migration in the target organism, and a chimeric protein encoded at least in part by at least one of the foregoing and introduced into the target organism, the polynucleotide coding sequence being under transcriptional control of a promoter active in a tissue located
15 sufficiently close to the developing gonadal cell so as to signal the cell to migrate.

7. A method as claimed in Claim 6, wherein the native polynucleotide coding sequence is *C. elegans* *gon-1*.

8. A method as claimed in Claim 6, wherein the
20 heterologous polynucleotide coding sequence is a homolog of *C. elegans* *gon-1*.

9. A method as claimed in Claim 8 wherein the homolog of *C. elegans* *gon-1* encodes a metalloprotease enzyme selected from the group consisting of murine ADAMTS-1
25 protein, bovine procollagen-1 N-proteinase, and human aggrecan-degrading metalloprotease.

10. A method as claimed in Claim 6 wherein the protein is truncated relative to a protein in a wild type individual.

11. A method as claimed in Claim 1 wherein the target organism is a nematode.

12. A method as claimed in Claim 11 wherein the target organism is a nematode selected from the group consisting 5 of ~~C. elegans~~ and ~~C. briggsae~~.

Sub B³ 13. A method as claimed in Claim 1 wherein ~~the at~~ least one modulator is selected from the group consisting of a nucleic acid molecule, a protein molecule, a sugar, a lipid, an organic molecule, a synthetic or natural 10 pharmaceutical agent, and a mixture thereof.

14. A method for identifying a nucleic acid sequence that affects migration of a developing gonadal cell, the method comprising the steps of:

treating a target organism by a method selected from 15 the group consisting of RNA interference, reverse genetics, and chemical mutagenesis to alter migration or shape of the developing gonadal cell in the treated target organism relative to migration in the target organism before treatment; and

20 identifying in the treated target organism a nucleic acid sequence affected by the treating step.

15. A method as claimed in Claim 14 wherein the treating step affects a nucleic acid sequence that encodes a protein.

16. A method as claimed in Claim 14 wherein the
treating step affects a nucleic acid sequence that
regulates nucleic acid transcription or translation.

17. A method as claimed in Claim 14 wherein migration
5 of the developing gonadal cell in the target organism
before treatment is absent or reduced relative to a wild
type individual.

18. A method as claimed in Claim 14 wherein the
treating step restores or enhances migration of the
10 developing gonadal cell in the treated target organism
relative to migration before the treating step.

19. A method as claimed in Claim 14 wherein migration
of the developing gonadal cell in the target organism
before treatment is at a level of a wild type individual.

15 20. A method as claimed in Claim 14 wherein the
treating step reduces migration of the developing gonadal
cell in the treated target organism relative to migration
before the treating step.

21. A method as claimed in Claim 14, wherein the target organism comprises a protein that directs cell migration, the protein being selected from the group consisting of a protein encoded by a native polynucleotide 5 coding sequence, a protein encoded by a heterologous polynucleotide coding sequence introduced into the target organism, a protein that shares at least 20% amino acid sequence identity with either of the foregoing and retains an ability to direct cell migration in the target organism, 10 and a chimeric protein encoded at least in part by at least one of the foregoing and introduced into the target organism, the polynucleotide coding sequence being under transcriptional control of a promoter active in a tissue located sufficiently close to the developing gonadal cell 15 so as to signal the cell to migrate.

22. A method as claimed in Claim 21 wherein the native polynucleotide coding sequence is *C. elegans gon-1*.

23. A method as claimed in Claim 21 wherein the heterologous polynucleotide coding sequence is a homolog of 20 *C. elegans gon-1*.

24. A method as claimed in Claim 23 wherein the homolog of *C. elegans gon-1* encodes a metalloprotease enzyme selected from the group consisting of murine ADAMTS-1 protein, bovine procollagen-1 N-proteinase, and human 25 aggrecan-degrading metalloprotease.

25. A method as claimed in Claim 21 wherein the protein is truncated relative to a protein in the wild type individual.

26. A method as claimed in Claim 14 wherein the target organism is a nematode.

27. A method as claimed in Claim 26 wherein the target organism is a nematode selected from the group consisting
5 of *C. elegans* and *C. briggsae*.